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# A high loading sulfonic acid-functionalized ordered nanoporous silica as an efficient and recyclable catalyst for chemoselective deprotection of *tert*-butyldimethylsilyl ethers

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**Abstract**—A high loading sulfonic acid-functionalized ordered nanoporous silica efficiently catalyzes the deprotection of a variety of alcoholic TBDMS (*tert*-butyldimethylsilyl)ethers in methanol. The catalyst shows high thermal stability (up to 240 °C) and can be recovered and reused for at least seven reaction cycles without loss of reactivity. This method can be used to deprotect TBDMS ethers of alcohols in the presence of TBDMS ethers of phenols.

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The role of silyl groups has been recognized as an important part of organic chemistry from both analytical and synthetic points of view, for example, as protecting groups in many syntheses of reasonable complexity.[1] *tert*-Butyldimethylsilyl (TBDMS) ethers are among the most frequently used protective groups for alcohols, because they can be easily installed in high yields and can withstand a wide variety of reaction conditions.[2] Although, the major goal of such a protection is usually to prevent unfavorable reactions of hydroxyl groups, in many cases it is often necessary to convert selectively the silyl ethers to their corresponding parent alcohols.[3] The usual procedure for deprotection of TBDMS ethers involves the use of $n$-$Bu_4N^+F^-$.[2a,4] However, fluoride-based protocols suffer from some disadvantages such as high cost of the reagent and incompatibility with base-sensitive substrates owing to the high basicity of fluoride ions, which can cause side reactions.[5] Thus, many alternative and mild protocols have been reported for the deprotection of silyl ethers and Lewis acid-based protocols using TMSOTf,[6] TMSCl,[7] $BF_3{\cdot}OEt_2$,[8] $BCl_3$,[9] $Sc(OTf)_3$,[10] $InCl_3$,[11] $ZnBr_2$,[12] $Zn(BF_4)_2$,[13] $Ce(OTf)_4$,[14] $CeCl_3{\cdot}7H_2O/NaI$,[15] $BiBr_3$,[16] $BiOClO_4$,[17] $SbCl_5$,[18] and $ZrCl_4$,[19] which have been developed for this purpose. Other milder reagents such as LiCl,[20] carboxylic acid resins,[21] organotin reagents,[22] $I_2$,[23] $n$-$Bu_4N^+$ $Br_3^-$,[24] NIS,[25] and acetonyl triphenylphosphonium bromide (ATPB)[26] have also been developed to desilylate TBDMS ethers under mild reaction conditions. Although, these methods are useful in many synthetic transformations, most of them suffer from limitations such as prolonged reaction times, formation of side products, the use of expensive catalysts, cumbersome work-up procedures, and the use of non-recyclable and sensitive catalysts. Therefore, it seems that there is much room for the development of new protocols to circumvent these problems.

Increasing awareness of the environmental costs of traditional acid-catalyzed chemical transformations has created an opportunity for new solid acid-based approaches for many important laboratory and industrial reactions.[27–31] Solid acids offer simpler and more benign alternatives than their homogeneous counterparts. However, to maintain economic viability, a suitable heterogeneous system must not only minimize the production of waste, but should also exhibit high stability, activities, and selectivities comparable or superior to the existing homogeneous routes. Polymer-supported catalysts have been widely used in research and in process chemistry due to easy recovery, however their use is restricted because of easy damage to the organic use polymer backbone (thermal or chemical).[32] One way to overcome this problem of the traditional polymer

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*Keywords*: Solid acids; Protecting groups; Solid sulfonic acids; TBDMS ethers; Catalysts.

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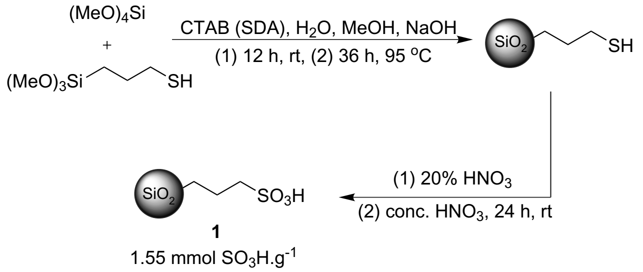
supported catalysts is to change the expensive organic polymer chain to a silica chain having a covalently anchored organic spacer to create organic–inorganic hybrid (interphase) catalysts.[33] In this type of solid, the reactive centers are highly mobile similar to that of homogeneous catalysts and at the same time it has the advantage of recyclability of the heterogeneous catalysts. Based on this idea, several types of sulfonic acid-functionalized silica have been synthesized and applied as alternatives to traditional sulfonic resins in catalyzing chemical transformations.[34] Among the different types of silica-based sulfonic acids, recently, Stein and his co-workers have prepared a novel sulfonic functionalized ordered microporous silicate, which shows high loading, high stability, and yet uniform nanostructure.[34j] However, to the best of our knowledge there is no report on the use of this catalyst for the deprotection of silyl ethers. The catalyst is made from a mixture consisting of (3-mercaptopropyl) trimethoxysilane (MPTS), tetramethoxysilane (TMOS), and cetyl trimethoxy ammonium bromide, (CTAB), as a template or structure directing agent (SDA). Extracted mecaptopropyl-MCM-41 was oxidized to the corresponding sulfonic acid derivative using $HNO_3$ as the oxidant (Scheme 1).[34j]

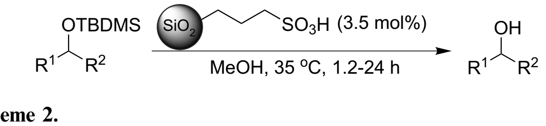
The organic composition of the solid sulfonic acid was quantitatively determined by thermogravimetric analysis (TGA) and ion-exchange *p*H analysis.[35] Typically a loading of ca. 1.55 mmol/g was obtained.

In continuation of this work, herein we wish to report a rapid and quite mild synthetic procedure for the cleavage of various types of TBDMS ethers using a trace amount (3.5 mol %) of solid sulfonic acid **1** (Scheme 2).

The catalytic properties of the catalyst were first tested in the deprotection of benzyl alcohol TBDMS ether. In this regard, we found that a small amount of catalyst **1** (23 mg, 3.5 mol % of $SO_3H$ groups) in methanol efficiently catalyzed the highly efficient deprotection of the TBDMS ether. We observed that the reaction was completed within 90 min and pure benzyl alcohol was obtained in 94% isolated yield (Table 1, entry 1).



**Scheme 1.**



**Scheme 2.**

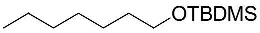
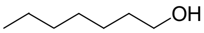
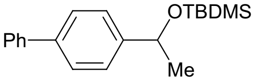
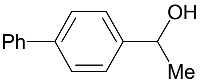
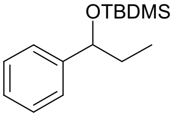
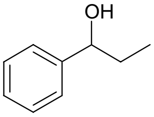
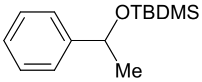
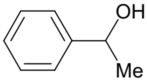
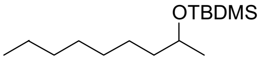
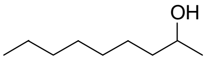
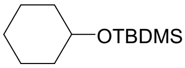
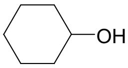
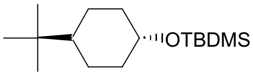
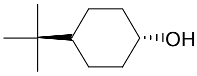
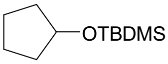
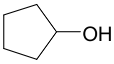
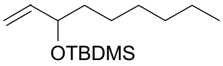
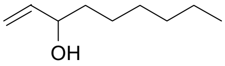
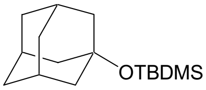
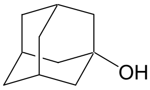
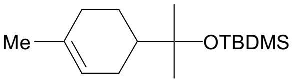
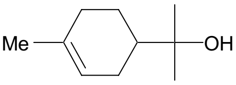
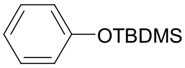
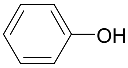
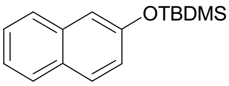
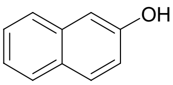
This result led us to examine the scope of this reaction for the deprotection of other silylated compounds. Our results show that the method is general for the cleavage of TBDMS ethers of primary (Table 1, entries 1–6), secondary (entries 7–13), allylic (entry 14), and hindered, acid sensitive secondary (entry 15) TBDMS ethers. We have also found that under similar reaction conditions even TBDMS-protected tertiary alcohols undergo deprotection to produce modest yields of the corresponding alcohols but longer reaction times were required than for less sterically hindered substrates (entries 16 and 17). Moreover, no elimination product was detected during the course of deprotection of tertiary TBDMS ethers (Table 1, entries 16 and 17). Inspection of the data in Table 1 also shows that the reaction conditions are mild enough to allow a C=C double bond to remain unaffected (entry 14). It should be noted that phenolic TBDMS ethers and *tert*-butyldiphenylsilyl (TBDPS) ethers (entries 18–20) are stable under the reaction conditions even when increasing the time or amount of catalyst **1**. This observation encouraged us to study the chemoselective deprotection of alcoholic TBDMS ethers in the presence of either TBDPS-protected alcohols or phenolic TBDMS ethers in competitive experiments. Indeed, our results show that this method is useful for the selective cleavage of alcoholic TBDMS ethers in the presence of TBDMS-protected phenols (Scheme 3).

Interestingly, our method can also be further extended to the chemoselective deprotection of TBDMS ethers in the presence of TBDPS ethers (Scheme 3). Such selectivity can be applied in syntheses in which two protected hydroxyl groups must be unmasked at different stages of the synthesis.

To demonstrate that the deprotection of silyl ethers catalyzed by the catalyst **1** is really a heterogeneous process, the deprotection of TBDMS-protected benzyl alcohol was carried out in MeOH in which the catalyst was filtered off at 55% conversion and the resulting clear solution surveyed for additional conversion in the absence of the solid. GC analysis of the reaction mixture after 4 h showed that no significant increase in the conversion level occurs after removal of the catalyst, thus indicating the solution does not contain any catalytically active species that could have leached from the solid to solution.

After having performed one reaction under the conditions described in Table 1, the catalyst was recovered by filtration, washed with an aliquot of fresh MeOH and $CH_2Cl_2$, dried, and then reused for a consecutive run under the same reaction conditions. Thus, after the first run, which gave the corresponding benzyl alcohol in 94% yield, after recovery, the catalyst was subjected to a second deprotection reaction from which it also gave the benzyl alcohol in 94% yield; the average chemical yield for seven consecutive runs was 92.5%,

**Table 1.** Selective deprotection of TBDMS ethers to the corresponding alcohols using nanoporous solid silica sulfonic acid in methanol at 35 °C

| Entry | Substrate | Product | Time (h) | Yield (%)[a,b] |
|---|---|---|---|---|
| 1 | $PhCH_2OTBDMS$ | $PhCH_2OH$ | 1.5 | 94 |
| 2 | 4-*i*-*Pr*$C_6H_4CH_2OTBDMS$ | 4-*i*-*Pr*$C_6H_4CH_2OH$ | 1.5 | 95 |
| 3 | $4\text{-}NO_2C_6H_4CH_2OTBDMS$ | $4\text{-}NO_2C_6H_4CH_2OTBDMS$ | 3 | 90 |
| 4 | $PhCH_2CH_2CH_2OTBDMS$ | $PhCH_2CH_2CH_2OH$ | 1.3 | 95 |
| 5 | $PhCH_2CH_2OTBDMS$ | $PhCH_2CH_2OH$ | 1.5 | 98 |
| 6 |  |  | 1.2 | 93 |
| 7 |  |  | 11 | 90 |
| 8 |  |  | 12 | 87 |
| 9 |  |  | 1.2 | 98 |
| 10 |  |  | 4.5 | 94 |
| 11 |  |  | 3.2 | 90 |
| 12 |  |  | 3.2 | 95 |
| 13 |  |  | 2.5 | 90 |
| 14 |  |  | 9 | 88 |
| 15 | $Ph_2CH–OTBDMS$ | $Ph_2CH–OH$ | 7 | 60[c] |
| 16 |  |  | 24 | 50[d] |
| 17 |  |  | 24 | 48[d] |
| 18 |  |  | 24 | 10[d,e] |
| 19 |  |  | 24 | 10[d,e] |
| 20 | $PhCH_2CH_2CH_2OTBDPS$ | $PhCH_2CH_2CH_2OH$ | 24 | 0[d,e] |

[a] Yields refer to isolated pure products unless otherwise stated.

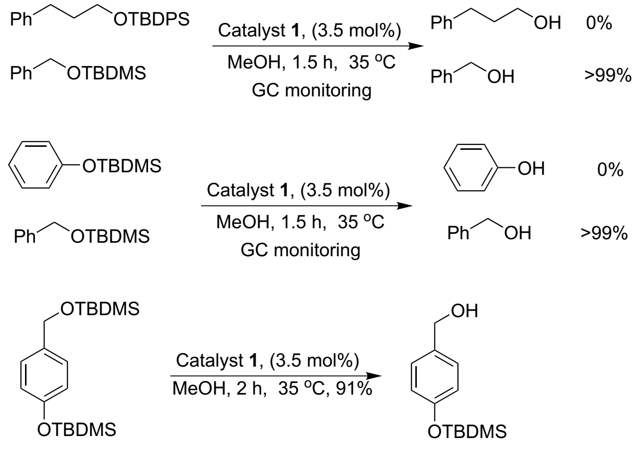
[b] The ratio of TBDMS ether:catalyst **1**:MeOH was 1:0.035:3 mL, respectively, and the reactions were performed 35 °C.

[c] Upon increasing the reaction time the corresponding benzhydrylmethyl ether was formed as a by-product.

[d] GC yield.

[e] The ratio of TBDMS or TBDPS ether:catalyst **1**:MeOH was 1:0.1:3 mL, respectively.

which clearly demonstrates the practical recyclability of this catalyst (Fig. 1). This reusability demonstrates the high stability and turnover of solid silica based sulfonic acid **1** under the conditions employed.



**Scheme 3.**

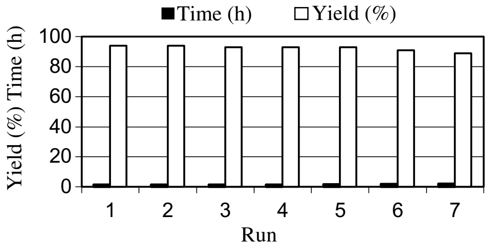


**Figure 1.** Recyclability of sulfonic acid catalyst for the deprotection of benzyl alcohol TBDMS ether.

A typical procedure for deprotection of TBDMS ethers to the corresponding alcohol is as follows: To a solution of TBDMS ether (1 mmol) in methanol (3 mL) the catalyst **1** (23 mg, 3.5 mol %) was added. The mixture was stirred at 35 °C for the period of time indicated in Table 1. Reaction progress was monitored by GC or TLC. After completion of the reaction, the product was isolated by simple filtration. Evaporation of the solvent under reduced pressure gave the corresponding alcohol in good to excellent yields (Table 1).

In conclusion, the sulfonic acid functionalized nanoporous silica **1**, which can be prepared simply from commercially available and relatively cheap starting materials, is an efficient, thermally stable (up to 240 °C), and recoverable catalyst for the deprotection of alcoholic TBDMS ethers in methanol at 35 °C. The reaction is selective for deprotection of alcoholic TBDMS ethers in the presence of either TBDMS ethers of phenols or TBDPS-protected alcohols. To the best of our knowledge, this protocol is the first example of deprotection of TBDMS ethers in which the catalyst can be recovered and reused over several reaction cycles without considerable loss of reactivity. We are currently exploring further applications of this solid sulfonic acid for other types of functional group transformations in our laboratories.

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## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.04.100.

## References and notes

1. (a) Greene, G. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, 1999; (b) Lalonde, M.; Chan, T. H. *Synthesis* **1985**, 817–845; (c) Kocienski, P. J. In *Protective Groups*; Enders, R., Noyori, R., Trost, B. M., Eds.; Thieme: Stuttgart, 1994.
2. (a) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191; (b) Chaudhury, S. K.; Hernandez, O. *Tetrahedron Lett.* **1979**, *20*, 99–102; (c) Corey, E. J.; Cho, H.; Rucker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455–3458; (d) Lombord, L. *Tetrahedron Lett.* **1984**, *25*, 227–228.
3. (a) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic: New York, 1998; (b) Nelson, T. D.; Crouch, R. D. *Synthesis* **1996**, 1031–1069.
4. Hanessian, S.; Lavalle, P. *Can. J. Chem.* **1975**, *53*, 2975.
5. Clark, J. H. *Chem. Rev.* **1980**, *80*, 429–452.
6. Hunter, R.; Hinz, W.; Richards, P. *Tetrahedron Lett.* **1999**, *40*, 3643–3646.
7. Grieco, P. A.; Markworth, C. J. *Tetrahedron Lett.* **1999**, *40*, 665–666.
8. Jackson, S. R.; Johnson, M. G.; Mikami, M.; Shiokawa, S.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 2694–2697.
9. Yang, Y. Y.; Yang, W. B.; Teo, C. F.; Lin, C. H. *Synlett* **2000**, 1634–1636.
10. Oriyama, T.; Kobayashi, Y.; Noda, K. *Synlett* **1998**, 1047–1048.
11. Yadav, J. S.; Reddy, B. V. S.; Madan, C. *New J. Chem.* **2000**, *24*, 853–854.
12. Crouch, R. D.; Polizzi, J. M.; Cleiman, R. A.; Yi, J.; Romany, C. A. *Tetrahedron Lett.* **2002**, *43*, 7151–7153.
13. Ranu, B. C.; Jana, U.; Majee, A. *Tetrahedron Lett.* **1999**, *40*, 1985–1988.
14. Bartoli, G.; Cupone, G.; Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Procopio, A.; Sambri, L.; Tararelli, A. *Tetrahedron Lett.* **2002**, *43*, 5945–5947.
15. Bartoli, G.; Bosco, M.; Marcantoni, E.; Sambri, L.; Torregiani, E. *Synlett* **1998**, 209–211.
16. Bajwa, J. S.; Vivelo, J.; Slade, J.; Repic, O.; Blacklock, T. *Tetrahedron Lett.* **2000**, *41*, 6021–6024.
17. Crouch, R. D.; Romany, C. A.; Kreshock, A. C.; Menconi, K. A.; Zile, J. L. *Tetrahedron Lett.* **2004**, *45*, 1279–1281.
18. Gloria, P. M. C.; Prabhakar, S.; Lobo, A. M.; Gomes, M. J. S. *Tetrahedron Lett.* **2003**, *44*, 8819–8821.
19. Sharma, G. V. M.; Srinivas, B.; Krishna, P. R. *Tetrahedron Lett.* **2003**, *44*, 4689–4691.
20. Farras, J.; Serra, C.; Vilarrasa, J. *Tetrahedron Lett.* **1998**, *39*, 327–330.
21. Corey, E. J.; Ponder, J. W.; Ulrich, P. *Tetrahedron Lett.* **1980**, *21*, 137–140.
22. Scheidt, K. A.; Chen, H.; Follows, B. C.; Chemler, S. R.; Coffey, D. S.; Roush, W. R. *J. Org. Chem.* **1998**, *63*, 6436–6437.
23. Lipshutz, B. H.; Keith, J. *Tetrahedron Lett.* **1998**, *39*, 2495–2498.

24. Gopinath, R.; Patel, B. K. *Org. Lett.* **2000**, *2*, 4177–4180.
25. Karimi, B.; Zamani, A.; Zareyee, D. *Tetrahedron Lett.* **2004**, *45*, 9139–9141.
26. Khan, A. T.; Ghosh, S.; Choudhury, L. H. *Eur. J. Org. Chem.* **2004**, 2198–2204.
27. Olah, G. A.; Pradeep, S. I.; Prakash, G. K. S. *Synthesis* **1986**, 513.
28. Corma, A. *Chem. Rev.* **1995**, *95*, 559.
29. Herron, N.; Farneth, W. E. *Adv. Mater.* **1996**, *8*, 959.
30. Horsley, J. A. *CHEMTECH* **1997**, 45.
31. Corma, A.; Garcia, H. *Catal. Today* **1997**, *38*, 257.
32. Sherrington, D. C. Polymer-supported in Synthesis. In *Chemistry of Waste Minimization*; Clark, J. H., Ed.; Blackie Academic: London, 1995, pp 141–200.
33. (a) Lu, Z. L.; Lindner, E.; Mayer, H. A. *Chem. Rev.* **2002**, *102*, 3543; (b) Wight, A. P.; Davis, M. E. *Chem. Rev.* **2002**, *102*, 3589; (c) Clark, J. H.; Macquarrie, D. J. *Chem. Commun.* **1998**, 853.
34. (a) Mbaraka, I. K.; Radu, D. R.; Lin, V. S.; Shanks, B. H. *J. Catal.* **2003**, *219*, 329; (b) Diaz, I.; Marquez-Alvarez, C.; Mohino, F.; Perez-Pariente, J.; Sastre, E. *J. Catal.* **2000**, *193*, 283; (c) Diaz, I.; Marquez-Alvarez, C.; Mohino, F.; Perez-Pariente, J.; Sastre, E. *J. Catal.* **2000**, *193*, 295; (d) Wilson, K.; Lee, A. F.; Macquarrie, D. J.; Clark, J. H. *Appl. Catal., A.* **2002**, *228*, 127; (e) Das, D.; Lee, J.-F.; Cheng, S. *Chem. Commun.* **2001**, 2178; (f) Melero, J. A.; Stucky, G. D.; Van Grieken, R.; Morales, G. *J. Mater. Chem.* **2002**, *12*, 1664; (g) Clark, J. H. *Acc. Chem. Res.* **2002**, *35*, 791; (h) Margolese, D.; Melero, J. A.; Christiansen, S. C.; Chmelka, B. F.; Stucky, G. D. *Chem. Mater.* **2000**, *12*, 2448; (i) Van Rhijn, W. M.; De Vos, D. E.; Sels, B. F.; Bossaert, W. D.; Jacobs, P. A. *Chem. Commun.* **1998**, 317; (j) Lim, M. H.; Blanford, C. F.; Stein, A. *Chem. Mater.* **1998**, *10*, 467; (k) Yang, Q.; Kapoor, M. P.; Inagaki, S. *J. Am. Chem. Soc.* **2002**, *124*, 9694.
35. See supporting material for experimental details.